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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/645,415	08/24/2000	David G. Bermudes	8002-059-999	3240

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EXAMINER

SHUKLA, RAM R

ART UNIT PAPER NUMBER

1632

DATE MAILED: 05/15/2003

*[Handwritten signature]*

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/645,415

Applicant(s)

BERMUDES ET AL.

Examiner

Ram R. Shukla

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 05 February 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 2-14, 16, 26-28, 40, 49-61, 63, 72, 86, 94 and 100-141 is/are pending in the application.
- 4a) Of the above claim(s) See Continuation Sheet is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 2, 5-8, 12, 14, 16, 26, 29-32, 36, 38, 40, 49, 52-55, 59, 61, 63, 105, 118, and 131 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☒ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7, 10, 14.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

Continuation of Disposition of Claims: Claims withdrawn from consideration are 3,4,9-11,13,27,28,33-35,37,50,51,56-58,60,100-104,106-117,119-130 and 132-141.

### **DETAILED ACTION**

1. Applicant's election of the invention of group I in Paper No. 21, dated 2-5-03 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicants' election of anti-angiogenic factor as the primary effector molecule, endostatin as the species of anti-angiogenic factor, an animal as the organism from which the primary effector is derived and bacteriocin release factor as the secondary effector molecule is acknowledged.

2. Claim 3, 4, 9-11, 13, 27, 28, 33-35, 37, 50, 51, 56-58, 60, 100-104, 106-117, 119-130, 132-141 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species. Election was made **without** traverse in Paper No. 21.

3. Claims 2, 5-8, 12, 14, 16, 26, 29-32, 36, 38, 40, 49, 52-55, 59, 61, 63, 105, 118, and 131 drawn to an attenuated tumor bacteria comprising an anti-angiogenic factor as the primary effector molecule, an animal as the organism from which the primary effector molecule is derived and a bacteriocin release factor as the secondary effector molecule are instant consideration.

### ***Information Disclosure Statement***

4. The information disclosure statement filed 8-24-01 fails to comply with 37 CFR 1.98(a)(1), which requires a list of all patents, publications, or other information submitted for consideration by the Office. It is noted that the PTO-1449 or equivalent is also not provided.

### ***Oath/Declaration/Sp cification***

5. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the

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specification of in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The specific reference to any prior nonprovisional application must include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number.

In the instant case, the priority information listed in the first sentence of the specification and the priority information listed in the oath/declaration do not match.

The specification and the oath/declaration are objected to because the priority information listed in the first sentence of the specification and the priority information listed in the oath/declaration do not match.

Applicants are required to correct the priority information in the first sentence and the oath/declaration.

### ***Claim Rejections - 35 USC § 103***

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 2, 5-8, 12, 14, 16, 26, 29-32, 36, 38, 40, 49, 52-55, 59, 61, 63, 105, 118, and 131 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kaniga (US 6,537,558 b2, 3-25-03, filing date 3-31-1997) or Sizemore et al (US 6,410,012B1, 6-25-02, effective filing date 3-28-1997) or Pawelek et al (US 6,190,657, 2-20-01, effective filing date 1-7-1995) in view of Boehm et al Nature 390:404-407, 1997) and Hakkaart et al (Mol Gen Genet 183:326-332, 1981).

At the time of Kaniga et al taught attenuated bacteria with decreased virulence by mutation of regulatory poxR gene. The art also teaches that these

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bacteria can be used as a vaccine or as host for the expression of heterologous genes and proteins or to deliver DNA to cells (see the abstract). The art teaches to improve the efficiency of transfer of the vector by including different mutations that reduce vector or other DNA upon lysis (column 15, lines 10-33). Additionally, a bacterial promoter could be used upstream of the eukaryotic promoter. The art also discusses different bacteria and DNA molecules that can be used in the method (see columns 10-12), for example tumor antigens etc. It is noted that the bacterial vector is used with the premise that the bacteria invades a host cell and then lyse to liberate the transfer DNA vector present in the attenuated bacteria.

Sizemore et al teaches a method for delivering a desired functional DNA or antigen to cells using attenuated bacteria. The art also teaches using antimicrobial agents to lyse the bacteria allowing the delivery of the functional DNA into the cell (see the entire document).

Pawelek et al teaches isolation and use of super-infective, tumor-specific and attenuated strains of bacteria that are used for diagnosis and treatment of sarcomas, carcinomas and other solid tumor cancers. The art discusses different aspects of using bacteria as a vector system (see column 6 and 7). The art teaches delivery of gene products such as HSV thymidine kinase (HSV-TK), pro-drug converting enzyme etc. to tumor cells for cancer treatment (see columns 18-23). The art teaches the treatment of mice bearing melanoma tumors using the attenuated bacteria expressing HSV-TK (see the examples in columns 54-72).

These art does not teach a bacteria that comprises one or more nucleic acids that encodes a primary effector molecule that encodes an anti-angiogenic factor and a secondary effector molecule that is a bacteriocin releasing factor.

Boehm et al teaches therapy of cancer in mice bearing Lewis lung carcinomas with angiogenesis inhibitor- TNP470 (see the second paragraph in the right column on page 404). The art also teaches that endostatin, a potent angiogenesis inhibitor treated cancer without the tumors developing drug resistance (see the first paragraph in the right column on page 404, also see the figures 1-4).

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Hakkaarat et al teaches genes encoded by the bacterial plasmid Clo DF13 and that the protein H encoded by the plasmid causes bacterial cell lysis (see the abstract).

At the time of the invention, it would have been prima facie obvious for an artisan of ordinary skill in the art to modify the bacteria of Kaniga et al or Pawelek et al or Sizemore et al for expressing an anti-angiogenesis factor, such as endostatin and a factor that will help in lysis of the bacteria and use such bacteria for treating cancers with a reasonable expectation of success. The art of record teaches methods to make bacteria that express a therapeutic gene and also plasmids that encode the protein H that lyses bacteria. An artisan would have been motivated to make such bacteria and treat a tumor with the bacteria because the art of record, such as Pawelek et al or Sizemore et al or Kaniga et teach that attenuated bacteria can be used to specifically target tumor cells and because Boehm et al teaches that angiogenesis inhibitors such endostatin treat cancer without producing drug resistance. An artisan would have been motivated to express the bacteriocin release factor, such as that encoded by plasmid Clo DF13 because this would help in lysing the bacteria in a host cell.

8. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (703) 305-1677. The examiner can normally be reached on Monday through Friday from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for this Group is (703) 308-4242. The after-final fax number is (703) 87209307. Any inquiry of a general nature, formal

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matters or relating to the status of this application or proceeding should be directed to the William Phillips whose telephone number is (703) 305-3413.

Ram R. Shukla, Ph.D.

Primary Examiner

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**RAM SHUKLA**  
**PRIMARY EXAMINER**